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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,802	10/31/2003	Xiang-Yang Han		1194

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/697,802	HAN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *3,4,9,10,23,24,36,37 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,11-16,18-22,25-29,31-35 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of SEQ ID Nos: 42 and 82 in the reply filed on March 24, 2006 is acknowledged. Claims 3, 4, 9, 10, 23, 24, 36, 37 and 46 are withdrawn since they do not include the elected sequences.

Claim Rejections - 35 USC § 112

2. Claims 15, 17, 21, 30 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15, 17, 21, 30 and 34 contain the trademarks/trade names Blast™ and Prepman™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify something, but it is not clear what specific limitations are imposed by the terms Blast™ and Prepman™. Accordingly, the identification/description is indefinite.

Claim Objections

3. In claim 1 and many of the later claims, the word "complimentary" is used when probably "complementary" is meant. It is suggested that this be corrected.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2, 8, 22, 35, 41 and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus specifically includes "fragments" and "variations". Thus, applicant has express possession of only a particular set of

sequences, in a genus which comprises hundreds of trillions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the the primers as encompassing "fragments" or "variations" lack any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the specifically disclosed sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a "fragment" or "variation", without any definition of the particular changes being claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise "fragments" or "variations". Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 5-8, 11-16, 19-22, 25-29, 31-35 and 38-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Philipp et al (FEMS Microbiology letters (1995) 132:263-269) as evidenced by Heym et al (Lancet (1994) 344:293-298)

Philipp teaches a method of claims 1 and 16 for determining a bacterium species (see abstract) comprising:

(a) annealing a region of a nucleotide template to a specific oligonucleotide primer set comprising SEQ-FOR and SEQ-REV in a complementary fashion, said primer set designed to provide a product having a predetermined size dicated by a complimentary primer set (see page 265, column 2 and table 1, where Philipp teaches amplification of mycobacterium tuberculosis using fifteen different primer sets),

(b) amplifying said region of said nucleotide template to produce said product (see page 264, column 2, subheading "PCR amplification").

With regard to claims 2, 8, 22, 35, 41, 45, as drawn to the elected primers of SEQ ID NO: 42 and 82, the primers in table 1 comprise "fragments" of SEQ ID NO: 42 and 82 and represent "variations" of SEQ ID NO: 42 and 82. For example, the first primer to the gsa gene, cosmid B2168 amplifies a 617 bp fragment and has the sequence CACATG, which is a fragment of SEQ ID NO: 42 and which sequence is a variation of SEQ ID NO: 42. Similarly the next primer of the gsa gene has the sequence CTC, which is a fragment and variation of SEQ ID NO: 82).

With regard to claim 5, Philipp teaches determing the M. tuberculosis sequence (see page 264, column 2).

With regard to claims 6, 19, 31, 42, Philipp teaches amplification of regions with variability (see page 266, column 1, where primers were drawn to conserved regions in the gene).

With regard to claim 7, 32, Philipp amplified for 35 cycles (see page 264, column 2).

With regard to claims 11, 12, 25, 26, 38, 39, Philipp teaches PCR products of 617 basepairs, which is between 500 and 700 base pairs (see table 1).

With regard to claim 13, 27, 40, Philipp teaches PCR products of 1358 basepairs, which is between 1000 and 1700 basepairs (see table 1).

With regard to claim 14, 20, 33, Philipp teaches amplification of Mycobacterium tuberculosis (see page 264, column 2).

With regard to claim 15, 21, 34, Philipp teaches analysis using the BLAST program (see page 264, column 1).

With regard to claim 28, Philipp teaches extraction of DNA from cultured bacteria (see page 264, column 1, citing Heym et al for DNA preparation. Heym teaches analysis of clinical isolates which were cultured from patients (see page 294, column 2).

With regard to claim 29, Philipp compares PCR product size on ethidium bromide stained agarose gels to molecular weight ladders (see figure 2).

With regard to claim 43, 44, Philipp shows that some of the primer pairs are universal to two different Mycobacterium, but which result in species specificity

since the M. leprae and M. tuberculosis products differ in size (see page 266, column 1).

8. Claims 1, 2, 5-8, 11-14, 16, 18, 19, 20, 22, 25-29, 31-33, 35 and 38-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Sechi et al (Mol. Cell. Probes (1999) 13:141-146).

Sechi teaches a method of claims 1 and 16 for determining a bacterium species (see abstract) comprising:

(a) annealing a region of a nucleotide template to a specific oligonucleotide primer set comprising SEQ-FOR and SEQ-REV in a complementary fashion, said primer set designed to provide a product having a predetermined size dicated by a complimentary primer set (see page 142, column 2, where Sechi teaches amplification using the p95a nd p447 primers),

(b) amplifying said region of said nucleotide template to produce said product (see page 142, column 2).

With regard to claims 2, 8, 22, 35, 41, 45, as drawn to the elected primers of SEQ ID NO: 42 and 82, the P95 and P-447 primers comprise "fragments" of SEQ ID NO: 42 and 82 and represent "variations" of SEQ ID NO: 42 and 82. For example, p-95 has the sequence CAC, which is a fragment of SEQ ID NO: 42 and which sequence is a variation of SEQ ID NO: 42. Similarly the P-447 primer has the sequence CC, which is a fragment and variation of SEQ ID NO: 82).

With regard to claim 5, Sechi teaches determing the M. tuberculosis sequence (see page 143, column 2).

With regard to claims 6, 19, 31, 42, Sechi teaches amplification of regions with variability (see page 143, column 2, where primers were drawn to conserved regions in the gene).

With regard to claim 7, 32, Sechi amplified for 35 cycles (see page 142, column 2).

With regard to claims 11, 12, 25, 26, 38, 39, Sechi teaches PCR products of 571 basepairs, which is between 500 and 700 base pairs (see page 143, column 1).

With regard to claim 13, 27, 40, Sechi teaches PCR products of 920 basepairs, which is "approximately" 1000 basepairs (see page 143, column 1).

With regard to claim 14, 20, 33, Sechi teaches amplification of Mycobacterium tuberculosis (see page 143, column 1).

With regard to claim 18, Sechi teaches the specimen is derived from a liquid (see page 142, column 2).

With regard to claim 28, Sechi teaches extraction of DNA from cultured bacteria (see page 142, column 2, where Mycobacterial strains were grown in medium).

With regard to claim 29, Sechi compares PCR product size on ethidium bromide stained agarose gels to molecular weight ladders (see figure 1).

With regard to claim 43, 44, Sechi shows that the primer pair are universal to many different Mycobacterium (as well as other organisms as shown at page 143, column 2), but which result in species specificity (see page 144).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 17 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sechi et al (Mol. Cell. Probes (1999) 13:141-146) in view of Higgins et al (App. Environ. Microbiol. (2001) 67(11):5321-5324).

Sechi teaches the limitations of claims 1, 2, 5-8, 11-14, 16, 18, 19, 20, 22, 25-29, 31-33, 35 and 38-45 as discussed above. Sechi does not teach the use of the Prepman reagent.

Higgins teaches the use of the Prepman reagent (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the Prepman reagent in the method of Sechi since Higgins notes "In summary, the Prepman, instagene, Xtra Amp and Isocode paper methods all yielded PCR quality DNA from E. coli colonies and broth culture (see page 5323, column 2)." The ordinary practitioner would have been motivated to use the Prepman method by Higgins who notes that the method costs less than $1.80 per sample and is rapid with lower equipment and reagent requirements than other methods (see page 5323, column 2).

11. Claims 15, 21 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sechi et al (Mol. Cell. Probes (1999) 13:141-146) in view of Bramucci et al (U.S. Patent 6,608,190).

Sechi teaches the limitations of claims 1, 2, 5-8, 11-14, 16, 18, 19, 20, 22, 25-29, 31-33, 35 and 38-45 as discussed above. Sechi does not teach the use of the Blast analysis.

Bramucci teaches Blast analysis of determination of bacterial sequence (see column 10, "Therefore, sequencing amplified 16S rDNA from a new bacterial isolate enables one skilled in the art to use the new 16S rDNA sequence as the query sequence in a BLAST search of the GenBank nucleotide sequence database and determine if the 16S rDNA of the new bacterial isolate is similar to any 16S rDNA that has been previously isolated, sequenced, and deposited in GenBank. If the query 16S rDNA sequence is less than 97% identical to any 16S rDNA sequence previously known in the art, then the query sequence has probably been derived from a previously unrecognized bacterial species").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the analysis method of Bramucci in the detection method of Sechi in order to determine with which bacteria a particular sequence is associated. An ordinary practitioner would have been motivated to apply BLAST to analysis of bacterial isolates in order to determine the bacterial species since Bramucci expressly indicates that BLAST alignments will permit determination of species both known and unknown based upon percent homology.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637

5/2/06